chemotherapy with rituximab, carmustine, etoposide, cytarabine and melphalan. **Adjuvant immunotherapy** consisted of rituximab 375 mg/M^2 IV weekly and sargramostim 250 ug s.c. TIW during weeks 5 to 8 and 24 to 27 post transplant.
Results: Seven patients had successful mobilization (mean CD34/kg collected 12.5E6 and infused 9E6) and underwent transplant. Median time to neutrophil and platelet engraftment was 9 and 10 days respectively. Six patients are alive with no evidence of disease from 3 to 18 months post transplant. One patient relapsed at 11 months. 4/4 patients receiving at least once cycle of adjuvant immunotherapy developed grade 1 to 4 neutropenia from 3 to 34 weeks post adjuvant rituximab. Neutrophil counts recovered following treatment with G-CSF, but recurred in all 4 patients without additional exposure to rituximab. One patient who had engrafted platelets developed grade 2 thrombocytopenia on day 33 post transplant. Platelets spontaneously recovered.
Conclusions: Delayed-onset neutropenia is a known complication of rituximab. The incidence may be higher when rituximab is used following ASCT. It is not clear if the timing of rituximab administration post transplant or the concomitant use of sargramostim contributed to the high incidence of delayed neutropenia in this study. Larger studies and longer followup will be needed to determine if adjuvant immunotherapy decreases relapse.

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CONSOLIDATION THERAPY FOLLOWING AUTOLOGOUS STEM CELL TRANSPLANTATION FOR NON-HODGKINS AND HODGKINS LYMPHOMAS

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Purpose: To determine whether autologous stem-cell transplantation (ASCT) followed by consolidation with Rituximab or irradiation is superior to ASCT alone in adults with advanced or relapsed lymphoma.
Patients and Methods: Fourteen consecutive lymphoma patients were entered onto this prospective, single center, phase II study. Seventeen previously transplanted patients were used as historical controls with continuous follow-up. Patients with non-Hodgkin's lymphoma (NHL, n = 11) or Hodgkin's disease (HD, n = 3) received ASCT followed by consolidation with Rituximab (375 mg/m2/week x4, every 6 months x5) or irradiation (20-30 Gy) respectively.
Results: Age, diagnosis (NHL vs. HD), B symptoms, risk factors, LDH, previous treatment response and histological type were well balanced between the two groups. With a median follow-up of 21.3 months, the 30-month relapse rate was 23% and 53% (P = 0.045), disease-free survival was 70% and 41% (P = 0.03) and overall survival was 73% and 47% (P = 0.07) for the consolidation group and historical controls, respectively. A multivariate analysis showed that age ≥ 55 and abnormal pre-transplant LDH were predictors of poor outcome. When NHL patients were analyzed separately (n = 24), 30-month relapse rate was 27% and 63% (P = 0.08), disease free survival was 73% and 47% (P = 0.05) and overall survival was 70% and 40% (P = 0.06) for consolidation and control arms, respectively.
Conclusion: The use of ASCT followed by consolidation using Rituximab (NHL) or irradiation (HD) in adults with advanced lymphoma showed a markedly decreased relapse rate and improved disease free and overall survival compared with conventional ASCT. The NHL subgroup (Rituximab) also demonstrated that consolidation produced a marked advantage.

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COMBINED AMIFOSTINE AND CRYOTHERAPY FOR PREVENTION OF ORAL MUCOSITIS (OM) FOLLOWING HIGH DOSE CHEMOTHERAPY WITH MELPHALAN AND AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANT (HCT) FOR MULTIPLE MYELOMA (MM)

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OM is a major cause of morbidity following autologous HCT for MM. Amifostine is a free radical scavenger that reduces proinflammatory cytokine production. Cryotherapy causes vasoconstriction of vessels in the oral cavity. Randomized controlled trials have demonstrated a significant reduction in the severity and duration of OM when amifostine or cryotherapy is administered with high dose melphalan prior autologous HCT for MM. To date, no report has been made of outcomes when both treatments are used concurrently.

We performed 28 autologous HCTs on 21 patients with MM in an outpatient setting. Patients received amifostine 740 mg/m^2 24 hours prior to and immediately prior to melphalan (200 mg/m^2 for 19 patients and 140 mg/m^2 for 2 patients; dose dependent on renal function). Cryotherapy was administered for four hours beginning 30 minutes prior to the administration of melphalan. Six patients had a decline in systolic blood pressure of ≥ 20% of baseline following the administration of amifostine. Aggressive intravenous hydration and Trendeleberg positioning resulted in the rapid return to baseline blood pressure in all cases. Prehydration and holding antihypertensive medications for 24 hours prior to the first dose of amifostine reduced symptomatic hypotension.

No patient was admitted for OM. The one patient who required both total parenteral nutrition and narcotic analgesics for grade III OM did not remove his dentures during cryotherapy. One patient experienced grade II OM that was managed with oral narcotic analgesics. The remaining 19 patients experiencing either grade I (n = 1) or no (n = 18) OM. Combined amifostine and cryotherapy is a well-tolerated and effective method of reducing OM following high dose melphalan and autologous HCT for MM.

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AUTOLOGOUS STEM CELL TRANSPLANTATION IN PATIENTS WITH REFRACTORY OR RELAPSED HODGKIN DISEASE IN COLOMBIA

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Objectives: The aim of this study is to report outcomes of patients with Hodgkin Disease (HD) after high dose therapy and autologous Hematopoietic Stem Cell Transplantation (auto-HSCT) in a single center in Colombia.
Methods: One hundred four patients with relapsed or refractory HD were treated with auto-HSCT between 1994 and 2008. Clinical status previous to transplantation, and events as relapse or death were analyzed to establish 5 year Overall Survival (OS) and Event Free Survival (EFS).
Results: One hundred four patients have had 105 procedures (one patient with 2 auto-SCT). Thirty-five female and 69 male, 79 adults and 25 less than 16 years, with average age of 27.4 years (range 5 to 66 yrs). Forty-one patients (39,4%) with refractory disease, 21 with early relapse (20%) and 42 with late relapse (40,4%).

Clinical stage at diagnosis: I and IIA 24 patients (23%), IIB 28 patients (26.9%), IIIA 7 patients (6.7%), III B 21 patients (20%), stage IV 21 patients (20%) and (3 patients unknown). The source of cells was peripheral blood in 95 transplants (91.4%), bone marrow in 6 (5.7%) and combined in 2 procedures (1.9%) combined, (2 patients unknown).

The conditioning chemotherapy was BEAM in 56 transplants (53.3%), cyclophosphamyde-etoposide-melphalan in 26 (24.7%) and other protocols in 23 (21.9%) transplants. At the time of transplantation, 61 patients (58%) were in complete remission, 36 (34%) in partial remission and 5 (4.7%) with active disease.

Twenty nine patients had relapse, of them 11 are dead. Seven patients had non relapse mortality: 5 with infectious complications, 1 with colecistitis and 1 with graft failure. Two patients died for complications of a second neoplasm. The mortality in the first 100-days was 3% (3 patients with infectious complications). With a median of 971 days of follow-up (range 12 to 5587 days), 59 (56.7%) patients are in complete remission, 17 (16.3%) are alive after relapse, 21 (20.1%) have died and 7 (6.7%) were lost for follow-up.

Conclusions: Near 50% of patients with refractory or relapsed HD can be successfully treated with high dose chemotherapy and autologous stem cell transplantation.

It is important to have a longer follow up on these patients so we can perform analysis on prognostic factors for relapse and survival.

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EVALUATING EFFECTIVENESS OF CHANGING THE ADMINISTRATION TIME OF PLERIXAFOR ON PERIPHERAL CD 34 + CELL COUNTS

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Plerixafor has been shown to rapidly increase CD 34+ cells in healthy volunteers alone or in combination with Neupogen (Fowler, et al, 2009). The addition of Plerixafor to Neupogen results in a tripling of circulating CD34+ cells 10 hours after administration (Clerq, 2009).

At The Ohio State University Medical Center-James Cancer Hospital, we initially administered Plerixafor at 10 p.m. (10 hours prior to the start of Apheresis). Administering Plerixafor at this time created some issues requiring attention. First, there is the issue of inconvenience to the patient. The patient would come to the hospital at 9:45 p.m., get their dose, go home or to a local hotel, then return to the hospital for Apheresis at 7:30 a.m. the following morning. Secondly, because the outpatient clinic closed at 5:00 p.m., the patient would go to the inpatient unit and have the charge nurse administer the Plerixafor. At times, the inpatient unit had no available rooms to see the patient and observe for side effects, becoming a concern for the inpatient nursing staff to monitor the patient appropriately. Because of these issues, our institution changed the administration time of Plerixafor to 6:15 p.m. The outpatient clinic adjusted their clinic hours to accommodate the need for patients receiving Plerixafor.

Currently, we have administered Plerixafor to 24 patients (2 patients were remobilized with Plerixafor) since the drug received FDA approval in December, 2008. Nineteen patient received Plerixafor at 10 p.m. Of these, sixteen patients had an adequate peripheral CD 34+ count (>10) allowing them to collect an adequate amount of stem cells for transplant. Of the 5 patients that received Plerixafor at 6:15 p.m., 4 patients had an adequate peripheral CD 34+ cell count to proceed to Apheresis.

Changing the time of Plerixafor to 6:15 p.m. aided in the overall safety of the patient. It is less inconvenient for the patient to return to the hospital in the early evening (during daylight hours) and it allows for the outpatient nursing staff to address any issues in an appropriate setting.

Our institution is looking at other areas of improvement using Plerixafor. We are currently using an algorithm in determining which patients may not mobilize an adequate number of CD 34+ cells. Also, we are checking the peripheral CD 34+ cell count on day 4 of Neupogen in patients that are coming to the hospital to have their central line placed to assess the need for Plerixafor that evening.

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NEED OF RECONSIDERATION OF MOBILIZATION STRATEGY IN AUTOLOGOUS STEM CELL TRANSPLANTATION FOR MULTIPLE MYELOMA: RESULTS OF THE POSITIVE IMPACT OF HIGH NUMBER OF CD34 + INFUSED CELLS

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This study concerned 130 MM patients who underwent ASCT in our center between years 2000 and 2007. There were 79 males and 51 females with a median age of 56.8 years (34-72). Before transplantation, all patients received granulocyte-colony stimulating factor (G-CSF) 5μg/kg/day, PBSC were mobilized in steady state in 135 cases, 62 after G-CSF + cyclophosphamide. As conditioning, all pts received melphalan alone with a median total dose of 304 mg (130-440). Sixty six patients received a single ASCT and 64 patients received 2 ASCT in a double ASCT program. After transplantation, there were 2 graft failure, 40% of patients received red blood cell (RBC) transfusions (median number: 0 [0-23]), and 64% received platelet transfusions (median number: 1 [0-20]). The median number of days with neutrophils <0.5 G/L was 6 (0-33) and with platelets <20 G/L was 17 (2-104). The median length of hospitalization for auto transplantation was 18 days (14-54). To assess the impact of the infused CD34+ cells number, we have analyzed 2 groups: group 1 (n = 86) for ASCT with a number of CD34 + $\leq 3\times10^6$/kg and group 2 (n = 107) for ASCT with a number of CD34 + $>3\times10^6$/kg.

Results: We found a high significant impact of the high number of infused CD34+(group 2) on platelets recovery (p = 0.002). The univariate analysis using Cox model, showed a trend for the high number of infused CD34+ cells (group2) on leukocyte recovery O.R = 0.748 [0.5-1.0] (p = 0.0568) and a high significant impact of the same group on neutrophils recovery O.R = 0.670 [0.5-0.9] (p = 0.009). These results were not changed even after adjustment on age also on the sequential number of the ASCT in the double auto ASCT program. The multivariate analysis using Cox model, studying the impact of CD34+ group, age, gender, poor prognostic factors [high level of β2microglobulin and del(13)], mobilization (G-CSF alone or G-CSF + cyclophsphamide), showed a significant impact only of poor prognostic factors on overall survival O.R. = 7.94 [1.0-59.2] (p = 0.04) and also on progression free survival (PFS) O.R. = 2.55 [1.1-5.7] (p = 0.024).

Conclusion: High level of infused CD34+ appeared to be very optimal for hematological recovery after ATSC in MM, without any significant impact on O.S and PFS. An economical study is running on this population to assess the impact of this level on hospitalization and treatment costs, results will communicated in the future

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REVIEWING THE STATUS OF BACKUP HEMATOPOIETIC STEM CELLS (HSC) BANKING FOR MULTIPLE MYELOMA (MM) PATIENTS WHO ARE ELIGIBLE FOR AUTOLOGOUS HEMATOPOIETIC STEM CELLS TRANSPLANT (AHSCT) IN THIS POOR ECONOMY

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Novel drugs combinations have demonstrated response rates similar to AHSCT. Due to lack of long term follow up, impact of these novel agents on HSC mobilization is unknown. AHSCT is still standard therapy for newly diagnosed MM. There are randomized trials underway to better define the role and timing of AHSCT in MM. Due to this uncertainty with novel agents, arbitrary recommendations are made to cryopreserve backup stem cells for pts who want to postpone AHSCT & to collect additional HSC at 1st HSC collection for future use. There is no consensus on minimum duration of HSC cryopreservation, and this can create significant financial,legal & logistical issues for stem cell laboratories.

Methods: From 03/2000 to 06/2009, 270 MM pts were evaluated for AHSCT at Karmanos Cancer Center, Detroit, MI. This review was conducted to determine utilization of cryopreserved HSC for a 2nd AHSCT at relapse/progression. No stem cells were collected if the intent was not to offer AHSCT. Storage time was calculated as the time between 1st & 2nd BMTs; as time between BMT & death & as time between BMT & last follow-up for those known to be alive.

Results: Two hundred and fifty two eligible pts had HSC stored with the intent to immediately proceed with at least a single AHSCT. Seventeen pts (6.7%) received a 2nd transplant with progressive disease as the most common reason, tandem transplant and refractory disease being other causes to perform delayed AHSCT. Significantly more men than women received a second transplant. Differences in age, race and stage of disease were not statistically significant. The median CD 34^+ cells dose collected was 8×10^6/kg. A median 4.9 $x10^6$ CD 34^+ cells/kg were infused; 26% (66/252) of pts had no cells remaining after 1st transplant. Five (29%) of the 2nd transplants were done during the 6 months following the first transplant. The remainder occurred between 51 and 92 months following first transplant.